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Genetic Admixture in the Late Pleistocene

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ABSTRACT The replacement hypothesis of modern human origins holds that the original population of modern humans expanded throughout the world, replacing existing archaic populations as it went. If this expanding population interbred with the peoples it replaced, then some archaic mitochondria might have been introduced into the early modern gene pool. Such mitochondria would be recognizable today because they should differ from other modern mitochondria at several times the number of sites that we are used to seeing in pairwise comparisons. In this paper we ask what can be inferred from the absence of these "divergent" mitochondria from modern samples. We show that if the effective number of females in our species has been large for the past 40,000 years, then the level of admixture must have been low. For example, if this effective number exceeded 1.6 million, then we can reject the hypothesis that more more than 2/1,000 of the mitochondria in the early modern population derived from admixture with archaic peoples. We argue elsewhere that regional continuity would be detectable in the fossil record only if the rate of admixture exceeded 76%. Here, we show that this level of admixture would require the effective female size of the human population to have been less than 1,777 for the past 40,000 years.

Contemporary human mitochondrial DNA (mtDNA) is strikingly uniform. Published literature now includes data from several thousand mitochondria, all of them so similar that they might have come from a population of a few thousand individuals. This observation is puzzling if one accepts the multiregional hypothesis of modern human origins, which holds that the modern popultion descends from a widespread population that has occupied most of the Old World for over a million years (Frayer et al., 1993; Wolpoff, 1989; Wolpoff et al., 1988). To populate an area so large, the population must have numbered at least a few hundreds of thousands. A widespread population would also have been geographically structured, so its effective size would have been larger still (Nei and Takahata, 1993). If the effective female population size had been 500,000 for the past million years and 10,000 before that, then the expected time to a common ancestor would be about 70,000 generations or 1.4 million years.[1] Yet the low diversity in mitochondrial data implies that our common mitochondrial ancestor lived only a few hundred thousand years ago (Brown, 1980; Denaro et al., 1981; Cann et al., 1987; Maynard Smith, 1990; Excoffier and Langaney, 1989; Vigilant et al., 1991; Hasegawa and Horai, 1991; Ruvulo et al., 1993).

Our low mitochondrial diversity is less puzzling if one accepts the replacement hypothesis of modern human origins, which holds that all modern *Homo sapiens* are descended from a small population within the

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[1]This estimate is an average of 1,000 simulations with a sample size of 100. See Rogers (1995c) for a description of the algorithm.

last 100,000 years (Aiello, 1993; Stoneking, 1993; Stringer and Andrews, 1988; Cann et al., 1987; Harpending et al., 1993; Sherry et al., 1994; Rogers and Jorde, 1995; Rogers, 1995a). Low genetic diversity is exactly what this hypothesis predicts. Yet even if a replacement did occur, it is not clear that the replacement was complete. Smith (1991) has proposed that the invading modern population hybridized to some extent with the archaic peoples that it largely replaced. If so, we may one day discover one of their mitochondria in the modern gene pool. Such a mitochondrion would probably differ greatly from the others in our sample. If the archaic population were as large as we assumed in the preceding paragraph, then the expected time to the common ancestor of a random pair of archaic mitochondria would be more than 1.1 million years. The probability of this ancestor living within the past 500,000 years is less than 0.05.[2] On the other hand, genetic data indicate that the common ancestor of our existing mitochondrial sample lived within the past 200,000 years. Consequently, if archaic mitochondria exist in the modern gene pool, they probably differ from other modern mitochondria at several times the number of sites that we are used to seeing in pairwise comparisons. We will refer to such mitochondria as "divergent," and we emphasize that no one has ever found one. In what follows we use their apparent absence to test hypotheses about population history.

Suppose that an original small population of modern *Homo sapiens* expanded throughout the world mixing with surrounding peoples as it went. As a result of this admixture, a fraction q of the mitochondria in the early post-expansion population derived from the archaic populations that were (to a greater or lesser extend) replaced. Thus, q measures both the level of admixture and the initial frequency of divergent mitochondria in the post-expansion population of modern humans.[3] The replacement model holds that $q = 0$ (complete replacement), whereas the multiregional model holds that $q = 1$ (no replacement). Smith's hypothesis holds that q is less than unity but is still large enough to make regional continuity apparent in the fossil record. The question is, which hypotheses about q's value can be rejected, and which cannot?

A statistical hypothesis is tested by calculating its "tail probability"—the probability of an outcome at least as extreme as the outcome observed. The hypothesis is rejected if this probability is small. We are concerned here with the observation that the sample contains no divergent mitochondria. Since no smaller number of divergent mitochondria is possible, our tail probabilities are very simple: Under each hypothesis, we calculate the probability of observing no divergent mitochondria in a sample of size S. We reject those hypotheses that make this probability smaller than 0.05. Our calculations ignore the effect of mutation. This is reasonable because it would take several mutations to convert a nondivergent mitochondrion into a divergent one and this is unlikely to have occurred within the past 40,000 years. We also assume that recent mitochondrial evolution has been selectively neutral. This assumption is more troubling. For example, if the early modern population had possessed a selectively superior mitochondrion, then the absence of divergent mitochondria from modern samples could reflect their elimination by selection rather than a low rate of admixture. Consequently, our conclusions will be tentative pending further research into the effect of recent selection on the human mitochondrion.

Given these assumptions, there are just two sources of variation to consider. First, there is the problem of sampling from the modern gene pool. If x is the frequency of divergent mitochondria within the modern

[2]These results are based on 1 million simulations with a sample of size 2. In 95% of these simulations, the coalescence time exceeded 25,477 generations. The mean coalescence time was 56,630 generations.

[3]More precisely, if q is the initial frequency of mitochondria derived from admixture, then the initial frequency of divergent mitochondria is hq, where h is the fraction of archaic mitochondria that are detectably different. The preceding paragraph suggests that h will be close to unity, so we will lose little by ignoring the difference between q and hg. This will, however, introduce a small downward bias into our estimates of q.

gene pool, then the probability of finding none of them in a sample of size S equals

$$Q(x) = (1 - x)^S \approx e^{-Sx} \quad (1)$$

If $S = 5{,}000$, then $Q(x) < 0.05$ unless $x < 0.0006$, as shown by Stoneking (1993). Thus, we can reject the hypothesis that the frequency of divergent mitochondria in the modern gene pool exceeds 6 in 10,000.

But this does not justify the claim that the level of admixture 40,000 years ago was equally low. Over the millenia, genetic drift may have reduced (or inflated) the frequency of divergent mitochondria. To test hypotheses about the frequency just after the expansion, we must incorporate genetic drift into our statistical method. In a population with N_f females, the probability of observing no divergent mitochondria becomes

$$P(q) = \int_0^1 Q(x)\phi(x;q,t/N_f)dx + P_0(q,t/N_f) \quad (2)$$

where q is the level of admixture, t is the number of generations since the expansion, ϕ is the probability density of x over the range $0 < x < 1$ (Crow and Kimura, 1970, Eq. 8.4.6), and P_0 is the probability that $x = 0$ (Crow and Kimura, 1970, Eq. 8.4.12). The two terms in this expression account for the possibilities that : a) divergent mitochondria exist in the modern population but were missed by our sample, and b) there are none in the modern population. In Equation 2, the integral accounts for possibility a, and P_0 accounts for possibility b. The functions ϕ and P_0 are infinite series, which we approximate by summing their first 60 terms. Additional terms had no effect on the answers. When N_f is infinite, $P(q) = Q(q)$, and our calculations are based on Equation 1.

These equations allow us to calculate P for any given values of q and t/N_f. We assume that $t = 1{,}600$, i.e., that the expansion occurred 1,600 generations (40,000 years) ago. If the true figure were 80,000 years, all of the population sizes that we discuss would need to be doubled. For any given value of t/N_f, P is a declining function of q as shown in Figure 1. Thus, we can reject any hypothetical value of q that exceeds the point $\hat{q}$ at which $P(q) = 0.05$.

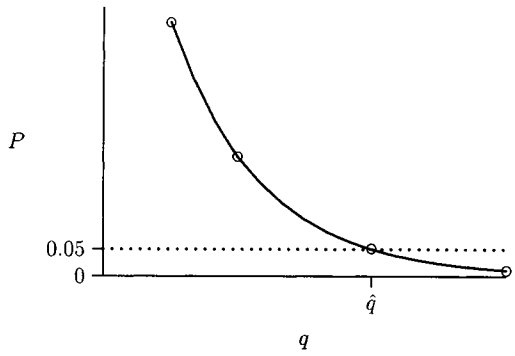

Fig. 1. Calculation of $\hat{q}$. All values of q greater than $\hat{q}$ can be rejected at the 0.05 significance level.

Equation 2 assumes that population size has been constant, yet in reality it has surely varied. We therefore interpret our N_f as referring to the minimum effective size over the past 40,000 years. Since $\hat{q}$ decreases with N_f, the true value of $\hat{q}$ will be somewhat smaller than the numbers we report. It will not be far off, however, because the long-term effective population size is much closer to the minimum size than to the average (Crow and Kimura, 1970).

This raises the possibility that the minimum size may have been very small at some time. We argue that this cannot be so if admixture took place throughout the world and if the human population has had a worldwide distribution ever since. When a worldwide population shrinks to a small size, it must either shrink to a single localized refuge or to several. If the population retains its worldwide distribution, then several refuges must be widely separated and therefore isolated from each other. Because of this isolation, such a population would have a large effective size even if each refuge were very small (Nei and Takahata, 1993). In such a population, the effect of drift on the frequency of divergent mitochondria could be large only if these divergent mitochondria occupied a single refuge. This is unlikely if admixture occurred throughout the world. Thus, our N_f cannot have been small in any generation if admixture was worldwide and

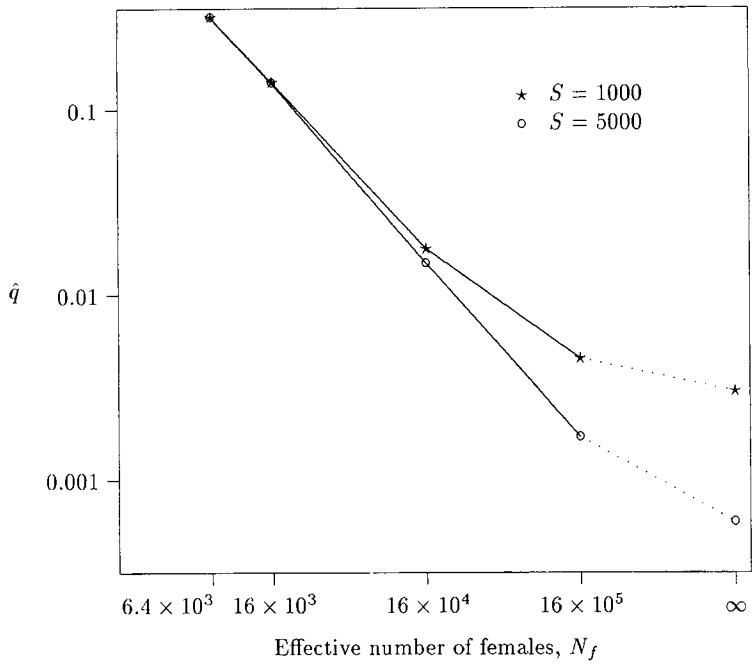

Fig. 2. What values of q can be rejected? For each combination of female popultion size N_f and a sample size S, $\hat{q}$ is the largest hypothetical value of q that cannot be rejected at the 0.05 significance level.

the human population has had a worldwide distribution ever since.

Figure 2 summarizes calculations of $\hat{q}$ under different assumptions about the population size N_f and the sample size S. The figure shows that $\hat{q}$ decreases as N_f increases. Consequently, any theory of modern human origins proposing substantial admixture (i.e., large q) must be compatible with small effective population size. The combination of large effective size and a high level of admixture is inconsistent with the data.

These results are consistent with the replacement model of modern human origins since we cannot reject the hypothesis that $q = 0$. The strong form of the multiregional hypothesis makes two claims that bear on our analysis. First, it implies that the world population was large, as we discussed above. Second, it claims that $q = 1$. These claims are inconsistent with the present results. On the other hand, Smith's variant of the multiregional hypothesis is harder to evaluate. It allows $q < 1$ and requires only that q be large enough to produce regional continuity in the fossil record. The question, then, is how large must q be to account for a level of continuity that could be observed in the fossil record?

To detect regional continutiy, it is necessary to demonstrate similarity between early and late fossil assemblages within regions. Since human fossils are scarce, these comparisons must be made using coarse geographic units—otherwise, the numbers within each region would be too small to be useful. In current literature, comparisons are made at the level of continents. This means that only three or four regions can be compared. One of us (Rogers, 1995b) has recently shown that when the number of regions is this small, it is unlikely that regional continuity will be detectable unless $q > 0.76$. If q is smaller than this, then the fossil evidence used to suport the multiregional model is unlikely to be statistically significant. Our calculations indicate that this would require an effctive population size of $N_f \leq 1{,}777$ females. Even if the actual number of females were five times the effective

number—as large, say, as the population of Concord township, Massachusetts—such population would be too small to populate all of Europe, Africa, and Asia. Thus, our results are inconsistent not only with the strong form of the multiregional hypothesis but also with Smith's weakened version, which allows for an expansion with admixture.

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